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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,356	05/09/2001	Martin A. Cheever	014058-009811US	1297

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER.**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	09/854,356	CHEEVER ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2006 and 16 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *113,114,116-125 and 145-156* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *113,114,116-125 and 145-156* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 113 and 116 are amended and new claims 155 and 156 added in the Response of 11/2/06. Applicants have not identified support for amended Claims 113 and 116 in the original specification.

Claims 113 and 116 recite "in a warm-blooded animal" which finds support, inter alia, at [0011 and 0038] of the specification; and

Claims 113 and 116 recite "wherein the immune response to HER-2/neu is elicited or enhanced in said animal" which finds support, inter alia, at [0003, 0012] of the specification;

Claims 113 and 116 recite "a protein comprising a contiguous amino acid sequence having SEQ ID NO: 6 (or 7)", respectively. The specification does not provide written description support for this recitation as discussed infra under "New Grounds for Rejection".

2. Claims 113, 114, 116-125 and 145-156 are all the pending claims for this application and all the claims under examination.

3. Applicants amendments to the claims have necessitated new grounds for rejection. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. The US patent and the nonpatent literature references cited in the IDS of 11/2/06 have been considered and entered.

Withdrawal of Rejections

35 USC §112, second paragraph

5. The rejection of Claims 113 and 116 for the recitation "capable of producing an immune response" is withdrawn in view of the deletion of the phrase from the claims and further in view of Applicants comments on p. 9, ¶7- p. 10, ¶2 of the Response of 11/2/06.

35 USC §112, first paragraph-enablement

6. The rejection of Claims 113, 116, 117-125 and 146-154 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn.

Applicant's arguments, see p. 10, ¶3- p. 13, ¶1, filed with the Response of 11/2/06, with respect to the rejection(s) of claim(s) 113, 116, 117-125 and 146-154 have been fully considered and are persuasive. Applicants allege "the present claims do not recite treatment of a particular disorder or cancer. The claims do not recite eliciting an immune response "against just any disorder". The present claims recite a method for "eliciting or enhancing an immune response to HER-2/neu protein" using a recited construct."

However, Applicants arguments as applied to Claims 114 and 145, which are drawn to vaccines, are not found persuasive. Further, upon consideration, a new ground of rejection is made in view of new Claims 155 and 156 drawn to humans.

35 USC § 102

7. The rejection of Claims 113, 114, 116, 118, 119, 121, 145-148 and 150 under 35 USC 102(e) as being anticipated by Cheever et al. (USPN 5,869, 445) is withdrawn. Applicant's arguments, see p, 5, ¶4- p. 8, ¶1, filed in the Response of 11/2/06, have been fully considered and are persuasive. Applicants allege "The cited Cheever reference does not teach a protein consisting of, or comprising, a contiguous series of amino acids having SEQ ID NO:6 (or SEQ ID NO:7)."

For these reasons, the rejection over Cheever is withdrawn.

8. The rejection of Claims 113, 114, 116, 118, 145 and 147 under 35 U.S.C. 102(e) as being anticipated by Laus et al. (USPN 5976546) is withdrawn. Applicant's arguments, see p. 13, ¶2-7, filed in the Response of 11/2/06, have been fully considered and are persuasive. Applicants allege "Comparing the full SEQ ID NO:4 of Laus to the present SEQ ID NO:6 (or 7) shows that while each sequence includes the extracellular domain of HER-2/neu, the polypeptides do not have the same contiguous amino acid sequence" and "nothing in Laus teaches or suggests a HER-2/neu construct comprising the Extracellular Domain joined directly to the Phosphorylation Domain (or any fragment of the Phosphorylation Domain).

For these reasons, the rejection over Laus is withdrawn.

35 USC 103(a)

9. The rejection of Claims 113 and 117 under 35 USC 103(a) as being unpatentable over Cheever et al. (USPN 5,869,445) in view of Forsgren (WO91/18926) is withdrawn. Applicant's arguments, see p. 8, ¶3-6, filed in the Response of 11/2/06, have been fully considered and are persuasive. Applicants allege "Cheever teaches a polypeptide having amino acids 676-1255 of HER-2/neu; nothing in Cheever teaches or suggests omitting amino acids 676-989 (more than half of Cheever's "preferred polypeptide") to obtain a polypeptide with immune enhancing properties. Forsgren does not teach HER-2/neu polypeptides."

For these reasons, the rejection over Cheever in view of Forsgren is withdrawn.

10. The rejection of Claims 113, 116, 119, 120, 122, 123, 124 and 149 and 151-153 under 35 USC 103(a) as being unpatentable over Cheever et al. (USPN 5,869, 445) in view of Garcon (WO95/1721) is withdrawn. Applicant's arguments, see p. 8, ¶1- p. 9, ¶2, filed in the Response of 11/2/06, have been fully considered and are persuasive. Applicants "refer to the discussions above regarding why Cheever does not anticipate or render obvious the present claims, and further submit that the teachings of Garcon do not remedy the deficiencies of the Cheever reference."

For these reasons, the rejection over Cheever in view of Garcon is withdrawn.

11. The rejection of Claims 113,116, 125 and 154 under 35 USC 103(a) as being unpatentable over Cheever et al. (US Patent 5,869, 445) in view of Krieg (WO

96/02555) is withdrawn. Applicant's arguments, see p. 9, ¶4-6, filed in the Response of 11/2/06, have been fully considered and are persuasive. Applicants "refer to the discussions above regarding why Cheever does not anticipate or render obvious the present claims, and further submit that the teachings of Krieg do not remedy the deficiencies of the Cheever reference."

For these reasons, the rejection over Cheever in view of Krieg is withdrawn.

Grounds for New Rejections

35 USC § 112-second paragraph

12. Claims 113, 114, 116-125 and 145-156 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 113, 114, 116-125 and 145-156 are indefinite for the recitation "a protein comprising a contiguous amino acid sequence" because in Claims 113 and 116, it is unclear what is meant by the phrase. The specification defines the term "contiguous" as "operably linked", for example, "in the case of secretory leaders in reading frame" [0150]. It is not clear whether and/or to what other protein the amino acid sequence of SEQ ID NO: 6 or 7 should be contiguous. A protein comprising a contiguous sequence of SEQ ID NO: 6 or 7 implies that the sequence of SEQ ID NO: 6 or 7 should be fused with another protein. Clarification is requested and required.

35 USC § 112-first paragraph

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 113, 114, 116-125 and 145-156 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

Claims 113, 114, 116-125 and 145-156 are drawn to methods for eliciting or enhancing an immune response to Her-2/neu protein comprising administering a

composition that comprises "a protein comprising a contiguous amino acid sequence having SEQ ID NO: 6" or "SEQ ID NO:7". The claims read on a genus of proteins which contain the contiguous amino acid sequence of SEQ ID NO:6 or 7. The specification teaches the full length Her-2/neu protein (SEQ ID NO:1) and two separate Her-2/neu fusion proteins comprising SEQ ID NO: 6 (919 amino acid residues; the extracellular domain (ECD) and the phosphorylation domain (PD) "of the human HER-2/neu protein (SEQ ID NO:6) and SEQ ID NO:7 (712 amino acid residues; the extracellular domain (ECD) and a preferred portion of the phosphorylation domain(ΔPD) of the human HER-2/neu protein (SEQ ID NO:7). The specification does not disclose or contemplate any other proteins which contain a stretch of amino acid residues of SEQ ID NOI:6 or 7. Therefore, the claims encompass a genus of proteins defined solely by a principal structural property, namely, that the protein contain a stretch of amino acids of SEQ ID NO: 6 or 7, and which is simply a wish to know the identity of any material with that structural property. Accordingly, there is insufficient written description encompassing a "protein comprising a contiguous stretch of amino acids of SEQ ID NO: 6 (or 7)" because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics of a "protein" are not set forth in the specification as-filed, commensurate in scope with the claimed invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification does

not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

In the absence of structural characteristics that are shared by members of the genus of a "protein" useful for eliciting or enhancing an immune response to Her-2/neu; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Enablement

14. Claims 114, 145, 155 and 156 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of eliciting an immune response using a Her-2/neu fusion protein comprising SEQ ID NOS: 6 or 7 to stimulate T-cell proliferation and cytotoxicity, and to induce B cells to produce an antibody, for use in treating malignancies such as breast, ovarian, colon, lung and prostate cancers, does not reasonably provide enablement for using the method to elicit a specific prophylactic or therapeutic immune response for any disease or disorder in a human. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 114 and 145 are drawn to a general method for eliciting or enhancing an immune response against Her-2/neu protein comprising administering a vaccine

composition comprising an isolated protein comprising a HER-2/neu fusion protein comprising an amino acid sequence comprising SEQ ID:6 (Claims 113, 114, 117-125) or SEQ ID NO:7 (Claims 116, 145-154). Claims 155 and 156 are drawn to the animal being human.

The Examiner's comments from the Office Action of 8/8/06 are incorporated by reference with respect to the vaccine claims, Claims 114 and 145. Further, the specification does not enable or support using the method of enhancing or eliciting the immune response where the composition is administered in the form of a vaccine. Two dictionary definitions (Stedman's Medical Dictionary and NCI Dictionary) of the term "vaccine" specifically require that a vaccine provide a prophylactic or therapeutic effect (see attached copies). The specification is not enabling for using the vaccine under any conditions where the prevention or treatment of any disease or disorder is observed. As stated previously, the specification teaches treating breast, ovarian, colon, lung and prostate cancers. There are no working examples in applicant's specification to guide the skilled artisan in practicing a method of eliciting or enhancing a specific preventative or therapeutic immune response to Her-2/neu for any kind of disorder or disease in a patient. Further, Applicants have not demonstrated an immune response eliciting or enhancing effect of the fusion protein of SEQ ID NO: 6 or SEQ ID NO:7 in a human, or with sufficient working examples of an animal model correlate.

In view of the undue experimentation that would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed

methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for eliciting or enhancing a specific preventative or therapeutic immune response in a subject much less that either protein of SEQ ID NO: 6 or 7 could elicit or enhance an immune response in a human, the enablement provided by the specification is not commensurate in scope with the claimed invention.

Conclusion

15. No claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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